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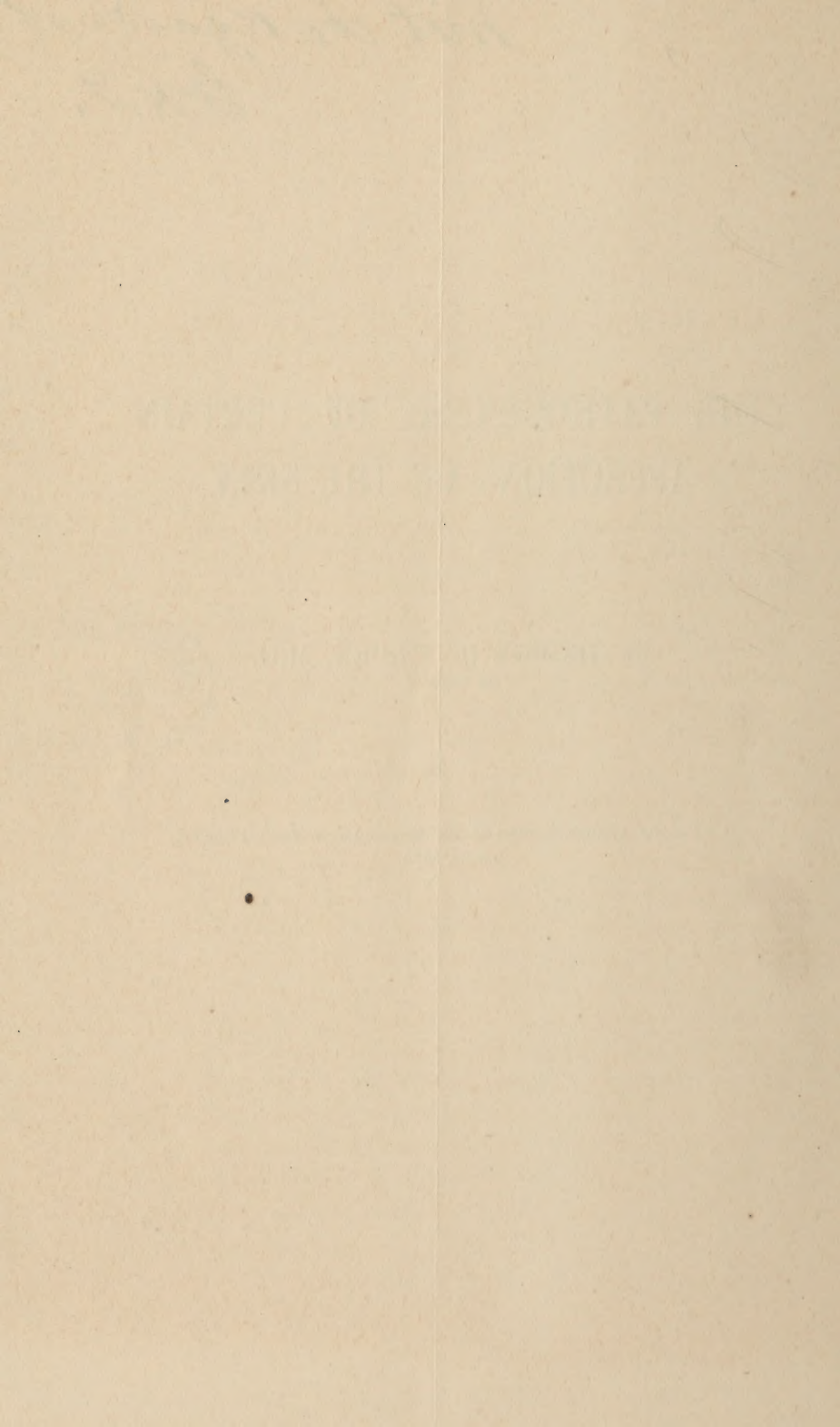
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THE PATHOGENESIS OF CERTAIN
AFFECTIONS OF THE SKIN.

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THE PATHOGENESIS OF CERTAIN AFFECTIONS OF THE SKIN. •

“Diseased nature oftentimes breaks forth in strange eruptions.”



It is well known that the introduction of various drugs into the stomach is sometimes followed by the appearance of a cutaneous eruption, and that the connection between them is one of cause and effect. One of the most common of the so-called medicinal eruptions, consisting of the acneiform, pustular and sometimes furuncular lesions due to the administration of the iodide or bromide of potassium, has been attributed to direct irritation of the glands of the skin because of the attempted cutaneous elimination of the drug from the system, and the detection of iodine and bromine in pus obtained from the cutaneous lesions gives to this idea apparent support. The histological character of such lesions, however, according to Duckworth, does not indicate that the cutaneous glands are primarily involved, while more recent microscopic investigation shows that although lesions caused by the internal use of iodine and bromine preparations may originate in dilatation and cellular infiltration of the capillary network which surrounds the sebaceous glands, the same process also affects bloodvessels which have nothing to do with the glandular apparatus of the skin, and may develop to such an extent that the consequent lesions represent a pustular dermatitis. The attribute of an eliminative pathogenesis, therefore, cannot be given to this variety of eruption

until more evidence in its favor is forthcoming, although the occasional inception of the process in the neighborhood of the cutaneous glands is suggestive of the ancient maxim, *ubi irritatio, ibi affluxus*.

Other forms of cutaneous lesions may also arise from the internal use of iodine and bromine compounds, and offer for consideration a large class of medicinal eruptions which differ in appearance from those just mentioned, and are independent of the physiological or therapeutic action of the drug to which they are due. They may be caused by many different drugs, and present a variety of forms, the most common and well recognized of which are as follows :

1.—Simple and evanescent erythematous patches, unattended by constitutional disturbance, and not apt to be followed by desquamation, which have been observed after the use of quinine, antipyrin, copaiba, iodide and bromide of potassium, cubebs and benzoate of soda.

2.—Papular erythematous lesions, attended with exudation into the cutaneous tissues, and resembling in some cases measles, in others the various forms of erythema multiforme, have been produced by the ingestion of quinine, antipyrin, copaiba and iodide of potassium.

3.—A diffuse form of erythematous dermatitis, not unfrequently accompanied by constitutional derangement, generally followed by desquamation and often closely simulating the rash of scarlet fever, has occurred in consequence of the administration of salicylic acid, quinine, opium, morphia and iodide of potassium.

4.—An urticarial eruption, consisting of wheals, is the most common of the medicinal eruptions, is apt to be combined with other forms and attended with constitutional disturbance, and has been described as following the use of copaiba, quinine, salicylic acid, antipyrin, iodide and bromide of potassium, opium, morphia, chloral hydrate and arsenic.

5.—Purpuric eruptions or circumscribed exudation of

blood into the dermal tissues, sometimes accompanied by hæmorrhages from the mucous membranes, are reported as having occurred from the use of quinine, salicylic acid, iodide of potassium and chloral hydrate.

Much less common than the above are :

1.—Bullos or pemphigoid eruptions. Such cutaneous lesions occurring after the use of iodide of potassium are rare, but well recognized, and isolated instances of the same are recorded as taking place after the use of bromide of potassium and copaiba.

2.—Vesicular eruptions resembling eczema have been described as following the use of various drugs, but they are exceptional, and the details with regard to them are meagre.

Attacks of typical herpes zoster are described by Hutchinson and others, as occurring during the administration of arsenic ; but it is a question whether such eruptions are not to be regarded as coincidences rather than consequent phenomena.

3.—A scaly eruption, resembling psoriasis, is mentioned by Gower as appearing, in three cases, during the administration of borax.

The drugs which are most apt to excite cutaneous eruptions, when given internally, are quinine, salicylic acid, copaiba, preparations of iodine and bromine, and it is worthy of notice that the new remedy antipyrin is especially prone to give rise to cutaneous manifestations, being followed by them, according to one observer, in ten per cent. of the cases in which it is used. Contrary to the opinion of Besnier, who supposed them to be due to reflex nervous disturbance, caused by gastric irritation, these eruptions may ensue, whether the drugs which excite them are introduced into the system by way of the stomach, by absorption through the mucous membrane of the rectum, by subcutaneous injection, or by contact with a wounded surface. They make their appearance shortly after absorption of the

drug has taken place, are acute, and run a rapid course in comparison with the pustular dermatitis due to iodine and bromine; are not unfrequently ushered in by a chill and accompanied by vomiting, headache and fever, offering a temporary but striking likeness to the acute exanthemata; are aggravated by the continuance or increase in the dose of the drug which causes them, and disappear upon its disuse. In some cases, however, the system seems to acquire a tolerance of the drug, and the cutaneous and other symptoms disappear notwithstanding its continued administration.

The pathogenesis of the medicinal eruptions is of importance as throwing light upon other and analogous pathological processes, but its nature is too complicated, and our knowledge too limited, to permit any such syllogistic and sweeping assertion of its neurotic character as has recently been made in the *Journal of Cutaneous and Venereal Diseases*.

With regard to the pustular lesions, so often caused by the use of iodine and bromine compounds, the evidence, taken for what it is worth, indicates that the changes in the skin are due to direct irritation of its tissues, on account of the presence therein of iodine and bromine—two very irritating substances. The deposition of finely divided metallic silver in the corium and consequent discoloration of the skin, which sometimes follows the long continued administration of nitrate of silver, demonstrates the possibility of the accumulation of a drug in the cutaneous tissues after its internal use, while the typical inflammatory and suppurative character of the lesions in question suggests reaction to direct irritation, and the detection of iodine and bromine furnishes the material for such irritation. In most cases these inflammatory changes in the skin do not appear until the drug has been taken for some time, and personal idiosyncrasy does not seem to play so prominent a part in their causation as in that of the other varieties of medicinal

eruptions, there not being manifest the same general condition of vascular irritability which is often connected with the latter. The production of the pustular dermatitis caused by iodine and bromine, seems rather to be a question of the amount of the drug received into the system compared with the individual's capacity for its elimination by the proper channels; an interesting fact in this connection being the observation, that in cases of Bright's disease, where the eliminating powers of the kidneys are crippled, this form of eruption takes place sooner and after smaller doses of the drug than usual.

As to the other varieties of medicinal eruptions, although they differ widely from each other in appearance, many of them are due to what looks like disturbance of the vasomotor system, and belong to the so-called angio-neurotic lesions of the skin, the type of which is furnished by the wheal of urticaria; and both Pellizzari and Erb call particular attention to the general and increased irritability of the cutaneous vascular system, which is present in these cases, a condition of things revealed by the ready formation of the so-called "taches cérébrales," first pointed out by Trousseau in connection with meningitis. Pathologically speaking, angio-neurotic lesions of the skin consist in various and varying degrees of dilatation of its capillaries, attended with more or less exudation of serum and wandering cells, separately or in combination, and such processes manifest themselves clinically by erythema of various types and urticarial eruptions. With regard to the bullous eruptions due to iodide of potassium, it may be stated that an angio-neurotic lesion of the skin, such as erythema or urticaria, may, by sudden and excessive exudation of serum, which causes the elevation of the epidermis "en masse," develop into a bullous eruption, and it is a question as to how many of these pemphigoid lesions are of this nature. For the production of the hæmorrhages into the cutaneous tissues

which take place in the purpuric eruptions, there is apparently necessary some change in the capillary walls themselves, for the red blood globule does not possess the power of amœboid movement which enables the white blood cell to migrate through the protoplasm, of which the walls of the capillaries are composed. This process is generally independent of any angio-neurotic manifestations, although it may be combined with them and thus give rise to a hæmorrhagic variety of such lesions. In what manner the presence of a drug, or some modification of the same, in the system, causes such pathological changes in the skin; whether by disturbance of the central or peripheral nervous system, by irritation of the capillaries themselves, or by a combination of the two processes, is a matter of speculation which is premature in proportion to the extent of our ignorance, but the truistic assertion may be made, that the entrance in some way into the circulatory system, of the drug which causes them, is requisite for the production of these eruptions. In any individual instance, the factor which seems to determine the morphology of the eruption is personal idiosyncrasy, or what Virchow has called, the "mystery of individuality," the same drug generally causing the same form of eruption in the same individual, and it is an interesting fact that such idiosyncrasy may be hereditary.

The entrance into the circulation of vaccine matter and so-called septic material is also competent to excite pathological changes in the skin. In vaccination, besides the more common and localized eruptions of erythema, eczema, and erysipelas, which start from the point of inoculation and spread by continuity, there sometimes occur exanthemata, which appearing after a certain period of incubation, upon regions of the body distant from the point of inoculation, often resemble in appearance angio-neurotic eruptions, and are apparently due to entrance into the circulation of vaccine matter, or possibly in some cases, as

Behrend supposes, of the products of suppuration which has taken place at the point of inoculation. During the course of diphtheria and other septic processes, and notably puerperal fever, there not unfrequently occur eruptions of the angio-neurotic type, being made up of erythematous and urticarial lesions, and probably the so-called puerperal scarlet fever and the "scarlet fever" after operations are of a septic nature and not genuine scarlatina. Bullous and very commonly purpuric lesions may also ensue in consequence of septic infection, and several observers have expressed the opinion that all cutaneous lesions, occurring as a result of such infection, are metastatic in character; and although this may not be true of all, it is not unlikely that the petechial lesions are of this nature, namely, hæmorrhagic infarcts of the skin caused by plugging of its capillary bloodvessels by emboli composed of micro-organisms, more especially as some recent microscopic observations, by Watson Cheyne, of the lesions occurring in purpura hæmorrhagica, seem to confirm this idea.

In the cases already considered, the foreign material or "*materies morbi*" which excites cutaneous manifestations of its presence in the system, is introduced into the organism from the outside, and this may also be said of the acute and contagious exanthemata, of typhus and typhoid fever, of glanders, of syphilis, of the oriental pest, and of infectious maladies, where cutaneous eruptions are exceptional and not characteristic of the disease, such as cholera, relapsing fever and acute miliary tuberculosis; but instances are not wanting in which similar appearances may be caused by the formation in the organism itself of material which by its presence in the blood is competent to give rise to changes in the skin, and examples of this are furnished by scurvy, uræmic poisoning and diabetes.

Chemical examination of scorbutic blood shows, besides other changes in its composition, increase in the amounts of

water, fibrin and albumen, and decrease in the quantity of its globular elements, and these changes which are apparently caused by exposure to hardship combined with deprivation of certain articles of diet, notably fresh vegetables, are attended by the development of purpuric lesions in the skin and hæmorrhages into other tissues of the body. There is no reason for supposing scurvy to be an infectious malady, and the suggestion that the purpuric lesions of the disease may be due to the influence of the same micro-organisms which are ordinarily harmless denizens of the mouth and other cavities of the body, but which in these cases are furnished with unusual opportunities for growth and development on account of the altered composition of the blood, is a curious instance of bacterio-mania.

In chronic diminution or complete arrest of the renal functions, the consequent retention in the blood of waste products which should be eliminated by the kidneys, usually manifests itself by headache, symptoms of gastric disturbance, and in severe cases by coma, but occasionally there are likewise produced cutaneous symptoms, consisting of a papular form of erythema, attended with exudation and followed by desquamation, which has been described under the name of erythema uræmicum. This form of eruption usually makes its first appearance upon the extremities, notably upon their extensor surfaces, and subsequently spreads to other parts of the body. Confluence of the original lesions sometimes causes the eruption to assume a likeness to that of scarlet fever, and in one case of unusual severity bullæ and purpuric lesions were formed in the skin and hæmorrhages took place into the mucous membrane of the mouth.

The cutaneous manifestations which occur during the course of diabetes, apparently in consequence of the over production of sugar in the system, have been made the subject of a special article by Kaposi, and may be of the angio-

neurotic type represented by roseola, erythema and chronic urticarial lesions, or of a more frankly inflammatory nature, consisting of furunculosis, carbuncular lesions and even gangrenous dermatitis. The presence of sugar has been demonstrated in these inflammatory lesions, which call to mind the similar cutaneous changes caused by iodine and bromine.

The eruptions which have thus far been mentioned are, properly speaking, not diseases *of* the skin, but changes *in* the skin, which are symptomatic of the presence in the circulation of some material which is foreign to the organism, and which either enters into it from without or is the result of perverted and incomplete performance of its physiological functions. In a crude way they may be arranged in three groups, namely, those of an angio-neurotic nature, represented by the various forms of erythema and urticaria; those of a reactive inflammatory and suppurative type, consisting in acneiform, furuncular and carbuncular lesions, and those of a hæmorrhagic variety, manifested by purpuric eruptions, and it is worthy of notice that eczema, which is so common a disease of the skin, is so rarely met with in this connection.

The pathological changes in the skin, which are regarded as cutaneous diseases properly so called, are not unfrequently purely symptomatic in their nature, and a rational method of treatment does not lose sight of this fact, although the exact indications to be met are often obscure or entirely unknown.

The acute outburst of urticaria, sometimes accompanied by vomiting and febrile symptoms, which occurs after the use of certain articles of food in susceptible individuals, has its exact counterpart in the similar eruption following the use of various drugs, and many strange examples of such personal and gastronomic idiosyncrasy are recorded. The typical and self-limited course of erythema multiforme, erythema nodosum, and certain varieties of purpura; the

prevalence of these diseases during the spring and autumn, the individual susceptibility which renders the patient liable to renewed attacks with the return of these seasons; the general feeling of languor and debility and arthritic pains which are often evident, and the occasional development of cardiac murmurs during the course of these maladies, all go to show that their cutaneous lesions are merely symptomatic of some general and possibly infectious influence, the exact nature of which is entirely hypothetical.

The chronic varieties of erythema and urticaria, on the other hand, which by recurring attacks form such an unpleasant feature in the existence of the sufferers therefrom, are symptomatic of some disturbance of the various physiological functions of the body, and external applications have upon them but a temporary and palliative effect. They may often be associated with manifest symptoms of dyspepsia, with costiveness and with improper modes of living, in which case the appropriate and generally effective remedy is to set right whatever is wrong, so far as lies in our power. The evil effects of the incomplete performance of the digestive and excretory functions are not limited to symptoms referred to various parts of the alimentary canal, and may even make themselves felt without any marked manifestations of the latter, and the lassitude, drowsiness and general debility so often met with in these cases are probably but milder manifestations of changes in the blood which may even result in symptoms of coma, such as have recently been described as following and probably caused by dyspepsia. A sedentary life in a vitiated atmosphere, and improper food, are to many the ordinary conditions of existence, and plenty of fresh air, physical exercise and regulation of the habits and diet are often more called for than drugs; but occasionally instances are met with where there is no obvious derangement of any but the cutaneous system, and where the functions of digestion and elimination are performed with regularity and apparent

completeness, and consequently our therapeutic efforts must sometimes be made at random. But the facts which come within the narrow limits of personal experience, that such cases are sometimes much relieved or even cured by the administration of salicylate of soda, atropia, or by a thorough going course of purgative waters, are suggestive of future possibilities in the way of therapeutics, when our knowledge of the action of drugs and the indications for their employment is more exact than it is at present. There is no doubt also that eczema and other cutaneous disorders which are not so purely symptomatic in their nature as those already mentioned, may be aggravated and kept up by similar conditions of the system, and a strict attention to the functional integrity and vigor of the body, in addition to local treatment, is often necessary to secure a successful result. Disturbance of the nervous system and exudative or inflammatory tissue changes are but the machinery of pathology, which is set in motion by what in the broadest sense of the word may be called irritation, and doubtless one form of such irritation is change in the composition of the blood by quantitative or qualitative modification of its various constituents, or by the introduction of foreign material, and the patient who makes the traditional demand for its purification may, in many cases, be nearer the source of his malady than the physician who is busy with the symptoms. However clumsy and ineffectual our therapeutic efforts may be, they should not be employed without a clear recognition of the close relations existing in matters of pathology between the body and its cutaneous envelope, which renders Dermatology, of all the special departments of medicine, the least independent of general pathological states of the system.

